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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,557	01/21/2004	D. James Surmeier	NWESTERN-08739	2838

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EXAMINER
CHONG, KIMBERLY

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,557	SURMEIER ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *0712/2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *4, 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 07/12/2007 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 03/09/2007 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 07/12/2007, claims 4 and 10 are pending in the application.

New Claim Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to convey to one skilled in the relevant art that the inventor(s) at the time the application was filed that applicant had possession of the claimed invention. This is a written description rejection.

Claims 4 and 10 are drawn to a method manipulating neuronal ion channels comprising transfecting a cell that expresses a mRNA encoding a Kv3.4 protein with a vector encoding an siRNA directed against said mRNA encoding a Kv3.4 protein wherein said siRNA is complementary to a portion of Kv3.4 mRNA found in Kv3.4a and absent in Kv3.4c and wherein said siRNA is capable of inhibiting Kv3.4 expression in said cell and wherein said cell is located *in vitro* or *ex vivo*.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Thus, an applicant complies with the written-description requirement by describing the invention, with all its claimed limitations, and by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical, structure/function correlation, methods of making the claimed product, and any combination thereof. The representative sample requirement may be satisfied by supplying structural or functional information, or a combination of both, such that one of skill in the art would be satisfied that applicants were in possession of the genus as claimed. Further, the size of the representative sample required is an inverse function of the unpredictability of the art.

At the outset it is noted that the rejected claims do not recite any sequence identifier relating to a Kv3.4 gene, specifically Kv3.4a, but rather refer to a broad genus of Kv3.4 and Kv3.4a genes.

The claims encompass a siRNA targeted to any Kv3.4 gene, as well as encompass any Kv3.4 homolog or allele from any species known or yet to be discovered of Kv3.4, as well as DNA genomic fragments, spliced variants or fragment that retains Kv3.4-like activity.

Although the specification discloses siRNA sequences having complementarity to a Kv3.4a, the specification does not describe siRNA sequences to any other species of Kv3.4 or Kv3.4a to describe the instantly claimed genus of all Kv3.4 or Kv3.4a genes. Each of the instantly disclosed siRNA is targeted to a single sequence, although the claims are drawn to any Kv3.4a sequence from any species. One of ordinary skill in the art could not make such siRNAs to any Kv3.4 or Kv3a gene without knowledge of the sequence. Given the breadth of sequences embraced in the instantly claimed genus, one could not envision the member siRNA that target such a broad genus.

Because the scope of the claimed invention is broad and the skilled artisan would not be able to envisage the entire genus claimed of siRNAs to any Kv3.4 or Kv3.4a gene, the skilled artisan would recognize that the applicant was in possession of the claimed genus at the time of filing. Not only do the claims broadly read on any Kv3.4 in any species, but additionally the skilled artisan would not be able to envisage which siRNA sequences would further result in inhibition of the Kv3.4 gene expression without undue experimentation.

Thus, the instantly claimed invention cannot be said to have been adequately described in a way that would convey with reasonable clarity to those skilled in the art that, as of the filling date sought, applicant was in possession of the claimed invention because the specification does not provide a description of a sufficient number of siRNA molecules to a sufficient number of Kv3.4 species that inhibit the expression of Kv3.4.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Retting et al. (cited on Applicant's IDS filed 11/23/2005), Low et al. (cited on PTO form 892 field 03/09/2007), Tuschl et al. (cited on PTO form 892 field 03/09/2007) and evidenced by Weiser et al. (cited on Applicant's IDS filed 11/23/2005).

Claims 4 and 10 are drawn to a method manipulating neuronal ion channels comprising transfecting a cell that expresses a mRNA encoding a Kv3.4 protein with a vector encoding an siRNA directed against said mRNA encoding a Kv3.4 protein wherein said siRNA is complementary to a portion of Kv3.4 mRNA found in Kv3.4a and absent in Kv3.4c and wherein said siRNA is capable of inhibiting Kv3.4 expression in said cell and wherein said cell is located *in vitro* or *ex vivo*.

Rettig et al. teach characterization of voltage-dependent potassium channels and the roles such channels play in cells. Rettig et al. specifically teach a potassium channel, described as Raw3, which is identified as a rapidly inactivating potassium channel (see page 2483). Rettig et al. teach cloning Raw3 cDNA into an expression vector and transfecting cells (see page 2478). It is recognized that Raw3 is known in the art as Kv3.4a (see Weiser et al., Table 1, page 951). Rettig et al. do not teach targeting Raw3 in a cell with a siRNA *in vitro* or *ex vivo* and do not teach transplanting the targeted cell into a subject.

Tuschl et al. teach siRNA molecules which are capable of mediating target-specific RNA interference and teach such siRNA molecules have improved safety and efficacy compared to therapeutic equivalents (see page 3, lines 12-16). Tuschl et al. teach siRNA can be expressed in a vector (see page 7, lines 17-23). Tuschl et al. teach such siRNA molecules can be used for determining the function of a gene in a cell by modulating the expression of said gene (see page 8, lines 11-13).

Low et al. teach a method of transfecting oligonucleotide compounds into cells *ex vivo* using an expression vector and teach transplanting said cells into a subject to be used as a vaccine to inhibit gene expression (see column 4, lines 6-60).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to target the Kv3.4a gene, as taught by Rettig et al. for the purpose of determining the function of said gene in a cell and further it would have been obvious for one of ordinary skill in the art to transfect siRNA into cells *ex vivo* and transplant said

cells into a subject to be used as a vaccine to inhibit gene expression, as taught by Low et al.

One would have been motivated to use a siRNA targeted to a Kv3.4a gene because Rettig et al. teach Raw3 potassium channel belongs to a class of rapidly inactivating A-type channels and of the Raw potassium channels, Raw3 is the only rapidly inactivating channel (see page 2483, column 1). Further, one would have been further motivated because Rettig et al. teach Raw3 plays an important role in the regulation of firing frequencies and action potential duration in neurons and teach Raw3 is of special interest because it is expressed in very distinct areas of the brain. One would have clearly been motivated to determine the function of Raw3 potassium channels the role expression of such protein plays in the central nervous system and one would have clearly used a siRNA particularly given that Tuschl et al. teach determining or modulating, particularly, inhibiting the function of a such a gene provide valuable information and therapeutic benefits in the filed of medicine (see page 8, lines 25- 28). Moreover, one would have been motivated to transfect cells ex vivo using a siRNA because Low et al. teach transfected cells can be efficiently transplanted into a subject and work to inhibit gene expression.

Finally, one would have a reasonable expectation of success at targeting a Raw3 gene given Rettig et al. teach the cDNA to said gene and Tuschl et al. teach the basic blue print of making and using siRNA to silence gene expression from any target gene of interest. Further, Low et al. teach efficient transplantation of cells transfected with an

antisense oligonucleotide and one would expect the same success using a siRNA since each molecule is a nucleic acid capable of inhibiting gene expression.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicant's Arguments

Re: Claim Rejections - 35 USC § 112

The rejection of record in the Office action filed 03/09/2007 of claims 4 and 10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is obviated in response to claim amendments filed 07/12/2007.

Re: Claim Rejections - 35 USC § 103

The rejection of record in the Office action filed 03/09/2007 of claims 4 and 10 under 35 U.S.C. 103(a) as being unpatentable over Chang et al. (J Oral Pathol Med. 2003, 32: 606-11, Low et al. (US Patent 6,071,891), Hammond et al. (Nature Reviews Genetics 2001, Vol. 2: 110-119) and Tuschl et al. (WO 02/44321) is obviated in response to claim amendments filed 07/12/2007 which deleted the rejected new matter and therefore Chang et al. is no longer available as prior art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service

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KC
Examiner AU 1635

/Sean McGarry/
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